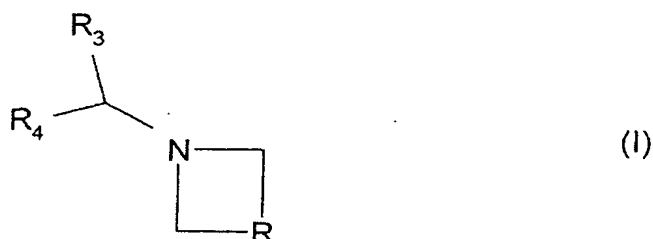


CLAIMS

1. A combination comprising one or more products  
which activate dopaminergic neurotransmission in  
the brain and of one or more CB1 antagonist  
5 azetidine derivatives of formula I:



wherein

**either A:**

- 10 R is  $CR_1R_2$ ,  $C=C(R_5)SO_2R_6$  or  $C=C(R_7)SO_2alk$ ; wherein  
either  $R_1$  is hydrogen and  $R_2$  is  
 $-C(R_8)(R_9)(R_{10})$ ,  $-C(R_8)(R_{11})(R_{12})$ ,  $-CO-NR_{13}R_{14}$ ,  
 $-CH_2-CO-NR_{13}R_{14}$ ,  $-CH_2-CO-R_6$ ,  $-CO-R_6$ ,  $-CO-$   
cycloalkyl,  $-SO-R_6$ ,  $-SO_2-R_6$ ,  $-C(OH)(R_{12})(R_6)$ ,  
15  $-C(OH)(R_6)(alkyl)$ ,  $-C(=NOalk)R_6$ ,  
 $-C(=NO-CH_2-CH=CH_2)R_6$ ,  $-CH_2-CH(R_6)NR_{31}R_{32}$ ,  $-CH_2-$   
 $C(=NOalk)R_6$ ,  $-CH(R_6)NR_{31}R_{32}$ ,  $-CH(R_6)NHSO_2alk$ ,  
 $-CH(R_6)NHCONHalk$  or  $-CH(R_6)NHCOalk$ ; or  
 $R_1$  is alkyl,  $NH-R_{15}$ , cyano,  $-S-alk-NR_{16}R_{17}$ ,  
20  $-CH_2-NR_{18}R_{19}$  or  $-NR_{20}R_{21}$ ; and  
 $R_2$  is  $-C(R_8)(R_{11})(R_{12})$ ;  
 $R_3$  and  $R_4$ , which are identical or different,  
independently are either alkyl, cycloalkyl,  
aryl chosen from phenyl, naphthyl or indenyl,  
25 wherein aryl being unsubstituted or  
substituted by one or more halogen, alkyl,  
alkoxy, formyl, hydroxyl, trifluoromethyl,  
trifluoromethoxy,  $-CO-alk$ , cyano,  $-COOH$ ,  
 $-COOalk$ ,  $-CONR_{22}R_{23}$ ,  $-CO-NH-NR_{24}R_{25}$ ,  
30 alkylsulfanyl, alkylsulfinyl, alkylsulfonyl,

- alkylsulfanylalkyl, alkylsulfinylalkyl,  
alkylsulfonylalkyl, hydroxyalkyl or -alk-  
NR<sub>24</sub>R<sub>25</sub>; or heteroaryl chosen from benzofuryl,  
benzothiazolyl, benzothienyl, benzoxazolyl,  
5 chromanyl, 2,3-dihydroxybenzofuryl,  
2,3-dihydrobenzothienyl, furyl, imidazolyl,  
isochromanyl, isoquinolyl, pyrrolyl, pyridyl,  
pyrimidinyl, quinolyl, 1,2,3,4-  
tetrahydroisoquinolyl, thiazolyl and thienyl,  
10 wherein heteroaryl is unsubstituted or  
substituted by one or more halogen, alkyl,  
alkoxy, hydroxyl, trifluoromethyl,  
trifluoromethoxy, cyano, -COOH, -COOalk,  
-CO-NH-NR<sub>24</sub>R<sub>25</sub>, -CONR<sub>22</sub>R<sub>23</sub>, -alk-NR<sub>24</sub>R<sub>25</sub>,  
15 alkylsulfanyl, alkylsulfinyl, alkylsulfonyl,  
alkylsulfanylalkyl, alkylsulfinylalkyl,  
alkylsulfonylalkyl or hydroxyalkyl;  
R<sub>5</sub> is hydrogen or alkyl;  
R<sub>6</sub> is Ar<sub>1</sub> or Het<sub>1</sub>;  
20 R<sub>7</sub> is cycloalkyl, heterocycloalkyl or  
heterocyclenyl optionally substituted by  
-CSO-phenyl;  
R<sub>8</sub> is hydrogen or alkyl;  
R<sub>9</sub> is -CO-NR<sub>26</sub>R<sub>27</sub>, -COOH, -COOalk, -CH<sub>2</sub>OH,  
25 -NH-CO-NH-alk, -CH<sub>2</sub>-NHR<sub>28</sub> or -NHCOOalk;  
R<sub>10</sub> is Ar<sub>1</sub> or Het<sub>1</sub>;  
R<sub>11</sub> is -SO<sub>2</sub>-alk, -SO<sub>2</sub>-Ar<sub>1</sub> or -SO<sub>2</sub>-Het<sub>1</sub>;  
R<sub>12</sub> is hydrogen, Ar<sub>1</sub> or Het<sub>1</sub>;  
R<sub>13</sub> is hydrogen or alkyl;  
30 R<sub>14</sub> is Ar<sub>1</sub>, Het<sub>1</sub>, -alk-Ar<sub>1</sub> or -alk-Het<sub>1</sub>;  
R<sub>15</sub> is alkyl, cycloalkyl or -alk-NR<sub>29</sub>R<sub>30</sub>;  
R<sub>16</sub> and R<sub>17</sub>, which are identical or different,  
independently are either hydrogen or alkyl;  
or

- 5           R<sub>16</sub> and R<sub>17</sub> taken together with the nitrogen atom to which they are attached form a saturated or unsaturated 3 to 10 ring membered mono- or 5 to 10 ring membered bicyclic heterocycle, optionally comprising one or more other heteroatoms chosen from oxygen, sulfur and nitrogen and optionally substituted by one or more alkyl;
- 10           R<sub>18</sub> is hydrogen or alkyl;
- R<sub>19</sub> is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, cycloalkylcarbonyl, -SO<sub>2</sub>alk, -CO-NHalk or -COOalk; or
- 15           R<sub>18</sub> and R<sub>19</sub> taken with the nitrogen atom to which they are attached form a saturated or unsaturated 3 to 10 ring membered mono- or 5 to 10 ring membered bicyclic heterocycle, optionally comprising one or more heteroatoms chosen from oxygen, sulfur and nitrogen and optionally substituted by one or more alkyl;
- 20           -NR<sub>20</sub>R<sub>21</sub> is a saturated or unsaturated monocyclic heterocycle having 3 to 8 ring members and optionally comprising another heteroatom chosen from oxygen, nitrogen and sulfur;
- 25           R<sub>22</sub> and R<sub>23</sub>, which are identical or different, independently are hydrogen or alkyl; or
- R<sub>22</sub> and R<sub>23</sub> taken together with the nitrogen atom to which they are attached form a saturated mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by one more alkyl;
- 30           R<sub>24</sub> and R<sub>25</sub>, which are identical or different, independently are hydrogen, alkyl, -COOalk,

cycloalkyl, alkylcycloalkyl, -alk-O-alk or hydroxyalkyl; or

5           R<sub>24</sub> and R<sub>25</sub> taken together with the nitrogen atom to which they are attached form a saturated or unsaturated and mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by one or more alkyl,  
10           -COalk, -COOalk, -CO-NHalk, -CS-NHalk, oxo, hydroxyalkyl, -alk-O-alk or -CO-NH<sub>2</sub>;

          R<sub>26</sub> and R<sub>27</sub>, which are identical or different, independently are hydrogen, alkyl, hydroxyalkyl, cycloalkyl, cycloalkylalkyl,  
15           -alk-COOalk, -alk-Ar<sub>1</sub>, alk-Het<sub>1</sub>, Het<sub>1</sub> or -alk-N(alk)<sub>2</sub>; or

          R<sub>26</sub> and R<sub>27</sub> taken together with the nitrogen atom to which they are attached form a saturated or unsaturated and mono- or bicyclic heterocycle having 3 to 10 ring members and optionally comprising one or more heteroatoms chosen from oxygen, sulfur and nitrogen and optionally substituted by one or more alkyl, alkoxy or halogen;  
20           R<sub>28</sub> is -CH<sub>2</sub>-alk, benzyl, -SO<sub>2</sub>alk, -CONHalk, -COalk, cycloalkylalkylcarbonyl, cycloalkylcarbonyl or -CO-(CH<sub>2</sub>)<sub>n</sub>OH, wherein n is an integer from 1 to 3;

25           R<sub>29</sub> and R<sub>30</sub>, which are identical or different, independently are hydrogen or alkyl; or

30           R<sub>29</sub> and R<sub>30</sub> taken together with the nitrogen atom to which they are attached form a saturated mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another  
35           heteroatom chosen from oxygen, sulfur and

nitrogen and optionally being substituted by one or more alkyl radicals;

$R_{31}$  and  $R_{32}$ , which are identical or different, independently are hydrogen, alkyl,  $Ar_1$  or

5         $-alk-Ar_1$ ; or

$R_{31}$  and  $R_{32}$  taken together with the nitrogen atom to which they are attached form a heterocycle chosen from aziridinyl, azetidiny, pyrrolidinyl and piperidinyl;

10         $Ar_1$  is phenyl or naphthyl optionally substituted by one or more substituents chosen from halogen, alkyl, alkoxy,  $-CO-alk$ , cyano,  $-COOH$ ,  $-COOalk$ ,  $-CONR_{22}R_{23}$ ,  $-CO-NH-NR_{24}R_{25}$ , alkylsulfanyl, alkylsulfinyl, alkylsulfonyl,

15        alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, hydroxyalkyl,  $-alk-NR_{24}R_{25}$ ,  $-NR_{24}R_{25}$ , alkylthioalkyl, formyl, hydroxyl,  $CF_3$ ,  $OCF_3$ ,  $Het_1$ ,  $O-alk-NH-cycloalkyl$  or  $SO_2NH_2$ ;

$Het_1$  is a saturated or unsaturated and mono- or

20        bicyclic heterocycle having 3 to 10 ring members and comprising one or more heteroatoms chosen from oxygen, sulfur and nitrogen and optionally substituted by one or more halogen, alkyl, alkoxy, alkoxycarbonyl,

25         $-CONR_{22}R_{23}$ , hydroxyl, hydroxyalkyl, oxo or  $SO_2NH_2$ ;

**or B:** wherein

$R$  is  $CHR_{33}$ ; wherein

$R_{33}$  is  $-NHCOR_{34}$  or  $-N(R_{35})-Y-R_{36}$ ;

30         $Y$  is  $CO$  or  $SO_2$ ;

$R_3$  and  $R_4$ , which are identical or different, are either aryl chosen from phenyl, naphthyl and indenyl, wherein aryl being unsubstituted or substituted by one or more halogen, alkyl,

35        alkoxy, formyl, hydroxyl, trifluoromethyl,

trifluoromethoxy, -CO-alk, cyano, -COOH,  
-COOalk, -CONR<sub>37</sub>R<sub>38</sub>, -CO-NH-NR<sub>39</sub>R<sub>40</sub>,  
alkylsulfanyl, alkylsulfinyl, alkylsulfonyl,  
alkylsulfanylalkyl, alkylsulfinylalkyl,  
5 alkylsulfonylalkyl, hydroxyalkyl or  
-alk-NR<sub>37</sub>R<sub>38</sub>; or heteroaryl chosen from  
benzofuryl, benzothiazolyl, benzothienyl,  
benzoxazolyl, chromanyl, 2,3-dihydro-  
benzofuryl, 2,3-dihydro-benzothienyl,  
10 pyrimidinyl, furyl, imidazolyl, isochromanyl,  
isoquinolyl, pyrrolyl, pyridyl, quinolyl,  
1,2,3,4-tetrahydroisoquinolyl, thiazolyl and  
thienyl, wherein heteroaryl being  
unsubstituted or substituted by halogen,  
15 alkyl, alkoxy, hydroxyl, trifluoromethyl,  
trifluoromethoxy, cyano, -COOH, -COOalk,  
-CO-NH-NR<sub>39</sub>R<sub>40</sub>, -CONR<sub>37</sub>R<sub>38</sub>, -alk-NR<sub>39</sub>R<sub>40</sub>,  
alkylsulfanyl, alkylsulfinyl, alkylsulfonyl,  
alkylsulfanylalkyl, alkylsulfinylalkyl,  
20 alkylsulfonylalkyl or hydroxyalkyl;  
R<sub>34</sub> is -alk-SO<sub>2</sub>-R<sub>41</sub>, -alk-SO<sub>2</sub>-CH=CH-R<sub>41</sub>, Het<sub>2</sub>  
substituted by -SO<sub>2</sub>-R<sub>41</sub> or phenyl substituted  
by -SO<sub>2</sub>-R<sub>41</sub> or -alk-SO<sub>2</sub>-R<sub>41</sub>;  
R<sub>35</sub> is hydrogen or alkyl;  
25 R<sub>36</sub> is phenylalkyl, Het<sub>2</sub> or Ar<sub>2</sub>;  
R<sub>37</sub> and R<sub>38</sub>, which are identical or different,  
independently are hydrogen or alkyl; or  
R<sub>37</sub> and R<sub>38</sub> taken together with the nitrogen atom to  
which they are attached form a saturated  
30 mono- or bicyclic heterocycle having 3 to 10  
ring members optionally comprising another  
heteroatom chosen from oxygen, sulfur and  
nitrogen and optionally being substituted by  
one or more alkyl;

- R<sub>39</sub> and R<sub>40</sub>, which are identical or different,  
independently are hydrogen or alkyl, -COOalk,  
cycloalkyl, alkylcycloalkyl, -alk-O-alk or  
hydroxyalkyl; or
- 5 R<sub>39</sub> and R<sub>40</sub> taken together with the nitrogen atom to  
which they are attached form a saturated or  
unsaturated and mono- or bicyclic heterocycle  
having 3 to 10 ring members optionally  
comprising another heteroatom chosen from  
10 oxygen, sulfur and nitrogen and optionally  
being substituted by one or more alkyl,  
-COalk, -COOalk, -CO-NHalk, -CS-NHalk, oxo,  
hydroxyalkyl, -alk-O-alk or -CO-NH<sub>2</sub>;
- R<sub>41</sub> is alkyl, Ar<sub>2</sub> or Het<sub>2</sub>;
- 15 Ar<sub>2</sub> is phenyl, naphthyl or indenyl radical, these  
radicals optionally being substituted by one  
or more halogen, alkyl, alkoxy, cyano, -CO-  
alk, -COOH, -COOalk, -CONR<sub>42</sub>R<sub>43</sub>, -CO-NH-NR<sub>44</sub>R<sub>45</sub>,  
alkylsulfanyl, alkylsulfinyl, alkylsulfonyl,  
20 -alk-NR<sub>44</sub>R<sub>45</sub>, -NR<sub>44</sub>R<sub>45</sub>, alkylthioalkyl, formyl,  
hydroxyl, hydroxyalkyl, Het<sub>2</sub>, -O-alk-NH-  
cycloalkyl, OCF<sub>3</sub>, CF<sub>3</sub>, -NH-CO-alk, -SO<sub>2</sub>NH<sub>2</sub>,  
-HN-COCH<sub>3</sub>, -NH-COOalk or Het<sub>2</sub> or else on two  
adjacent carbon atoms by a dioxymethylene;
- 25 Het<sub>2</sub> is a saturated or unsaturated and mono- or  
bicyclic heterocycle having 3 to 10 ring  
members and comprising one or more  
heteroatoms chosen from oxygen, sulfur and  
nitrogen optionally substituted by one or  
30 more alkyl, alkoxy, vinyl, halogen,  
alkoxycarbonyl, oxo, hydroxyl, OCF<sub>3</sub> or CF<sub>3</sub>,  
the nitrogenous heterocycles optionally being  
in their N-oxidized form;
- R<sub>42</sub> and R<sub>43</sub>, which are identical or different,  
35 independently are hydrogen or alkyl; or

R<sub>42</sub> and R<sub>43</sub> taken together with the nitrogen atom to which they are attached form a saturated mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by one or more alkyl;

R<sub>44</sub> and R<sub>45</sub>, which are identical or different, independently are hydrogen, alkyl, -COOalk, cycloalkyl, alkylcycloalkyl, -alk-O-alk or hydroxyalkyl; or

R<sub>44</sub> and R<sub>45</sub> taken together with the nitrogen atom to which they are attached form a saturated or unsaturated and mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by one or more alkyl, -COalk, -COOalk, -CO-NHalk, -CS-NHalk, oxo, hydroxyalkyl, -alk-O-alk or -CO-NH<sub>2</sub>;

**or C: wherein**

R is CHR<sub>46</sub>, wherein

R<sub>46</sub> is -N(R<sub>47</sub>)R<sub>48</sub>, -N(R<sub>47</sub>)-CO-R<sub>48</sub> or -N(R<sub>47</sub>)-SO<sub>2</sub>R<sub>49</sub>;

R<sub>3</sub> and R<sub>4</sub>, which are identical or different, represent either an aryl chosen from phenyl, naphthyl and indenyl, wherein aryl being unsubstituted or substituted by one or more halogen, alkyl, alkoxy, formyl, hydroxyl, trifluoromethyl, trifluoromethoxy, -CO-alk, cyano, -COOH, -COOalk, -CONR<sub>50</sub>R<sub>51</sub>, -CO-NH-NR<sub>52</sub>R<sub>53</sub>, alkylsulfanyl, alkylsulfinyl, alkylsulfonyl, alkylsulfanyllalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl, hydroxyalkyl or -alk-NR<sub>7</sub>R<sub>8</sub>; or a heteroaryl chosen from benzofuryl, benzothiazolyl,



benzothienyl, benzoxazolyl, chromanyl, 2,3-dihydrobenzofuryl, 2,3-dihydrobenzothienyl, furyl, imidazolyl, isochromanyl, isoquinolyl, pyrrolyl, pyridyl, pyrimidyl, quinolyl, 1,2,3,4-tetrahydroisoquinolyl, thiazolyl and thienyl, wherein heteroaryl being unsubstituted or substituted by halogen, alkyl, alkoxy, hydroxyl, trifluoromethyl, trifluoromethoxy, cyano, -COOH, -COOalk, -CO-NH-NR<sub>52</sub>R<sub>53</sub>, -CONR<sub>50</sub>R<sub>51</sub>, -alk-NR<sub>52</sub>R<sub>53</sub>, alkylsulfanyl, alkylsulfinyl, alkylsulfonyl, alkylsulfanylalkyl, alkylsulfinylalkyl, alkylsulfonylalkyl or hydroxyalkyl;

R<sub>47</sub> is -C(R<sub>54</sub>)(R<sub>55</sub>)-Het<sub>3</sub>, Het<sub>3</sub>, -C(R<sub>54</sub>)(R<sub>55</sub>)-Ar<sub>3</sub>, Ar<sub>3</sub>, cycloalkyl or norbornyl;

R<sub>48</sub> is hydrogen or hydroxyalkyl, -alk-COOalk, -alk-CONR<sub>50</sub>R<sub>51</sub>, -alk-NR<sub>50</sub>R<sub>51</sub>, alkoxy; Ar<sub>3</sub>, Het<sub>3</sub>, -CH<sub>2</sub>Ar<sub>3</sub>, -CH<sub>2</sub>Het<sub>3</sub> or alkyl, optionally substituted with one or more halogen;

R<sub>49</sub> is hydroxyalkyl, -alk-COOalk, -alk-CONR<sub>50</sub>R<sub>51</sub>, -alk-NR<sub>50</sub>R<sub>51</sub>, alkoxy, Ar<sub>3</sub>, Het<sub>3</sub>, -CH<sub>2</sub>Ar<sub>3</sub>, -CH<sub>2</sub>Het<sub>3</sub> or alkyl optionally substituted with one or more halogen;

R<sub>50</sub> and R<sub>51</sub>, which are identical or different, independently are hydrogen or alkyl; or

R<sub>50</sub> and R<sub>51</sub> taken together with the nitrogen atom to which they are attached form a saturated mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by one or more alkyl;

R<sub>52</sub> and R<sub>53</sub>, which are identical or different, independently are hydrogen or alkyl, -COOalk,

cycloalkyl, alkylcycloalkyl, -alk-O-alk or hydroxyalkyl; or

5 R<sub>52</sub> and R<sub>53</sub> taken together with the nitrogen atom to which they are attached form a saturated or unsaturated and mono- or bicyclic heterocycle having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and nitrogen and optionally being substituted by one or more alkyl,  
10 -COalk, -COOalk, -CO-NHalk, -CS-NHalk, oxo, hydroxyalkyl, -alk-O-alk or -CO-NH<sub>2</sub>;

R<sub>54</sub> is hydrogen, hydroxyalkyl, -alk-COOalk, -alk-CONR<sub>50</sub>R<sub>51</sub>, -alk-NR<sub>50</sub>R<sub>51</sub>, alkoxyalkyl, Ar<sub>3</sub>, Het<sub>3</sub>, -CH<sub>2</sub>Ar<sub>3</sub>, -CH<sub>2</sub>Het<sub>3</sub> or alkyl optionally  
15 substituted with one or more halogen;

R<sub>55</sub> is hydrogen or hydroxyalkyl, -alk-COOalk, -alk-CONR<sub>50</sub>R<sub>51</sub>, -alk-NR<sub>50</sub>R<sub>51</sub>, alkoxyalkyl or alkyl optionally substituted with one or more halogen; or

20 R<sub>54</sub> and R<sub>55</sub> taken together with the carbon atom to which they are attached form a saturated mono- or bicyclic ring having 3 to 10 ring members optionally comprising another heteroatom chosen from oxygen, sulfur and  
25 nitrogen and optionally being substituted by one or more alkyl;

Ar<sub>3</sub> is phenyl, naphthyl or indenyl, optionally being substituted by one or more halogen, alkyl, alkoxy, -CO-alk, cyano, -COOH, -COOalk, -CONR<sub>56</sub>R<sub>57</sub>, -CO-NH-NR<sub>58</sub>R<sub>59</sub>,  
30 alkylsulfanyl, alkylsulfinyl, alkylsulfonyl, -alk-NR<sub>58</sub>R<sub>59</sub>, -NR<sub>58</sub>R<sub>59</sub>, alkylthioalkyl, formyl, CF<sub>3</sub>, OCF<sub>3</sub>, Het<sub>3</sub>, -O-alk-NH-cycloalkyl, SO<sub>2</sub>NH<sub>2</sub>, hydroxyl, hydroxyalkyl, -NHCOalk or -NHCOOalk

or on 2 adjacent carbon atoms by  
dioxymethylene;

Het<sub>3</sub> is a saturated or unsaturated and mono- or  
bicyclic heterocycle having 3 to 10 ring  
5 members and comprising one or more  
heteroatoms chosen from oxygen, sulfur and  
nitrogen optionally substituted by one or  
more alkyl, alkoxy, halogen, alkoxycarbonyl,  
oxo or hydroxyl, the nitrogenous heterocycles  
10 optionally being in their N-oxidized form;

R<sub>56</sub> and R<sub>57</sub>, which are identical or different,  
independently are hydrogen or alkyl radical;  
or

R<sub>56</sub> and R<sub>57</sub> taken together with the nitrogen atom to  
15 which they are attached form a saturated  
mono- or bicyclic heterocycle having 3 to 10  
ring members optionally comprising another  
heteroatom chosen from oxygen, sulfur and  
nitrogen and optionally being substituted by  
20 one or more alkyl;

R<sub>58</sub> and R<sub>59</sub>, which are identical or different,  
independently are hydrogen or alkyl; or

R<sub>58</sub> and R<sub>59</sub> taken together with the nitrogen atom to  
25 which they are attached form a saturated  
mono- or bicyclic heterocycle having 3 to 10  
ring members optionally comprising another  
heteroatom chosen from oxygen, sulfur and  
nitrogen and optionally being substituted by  
one or more alkyl;

30 alk is an alkyl or alkylene radical; and wherein  
the alkyl, alkylene and alkoxy radicals have  
straight or branched chains and comprise 1 to  
6 carbon atoms, the cycloalkyl radicals  
comprise 3 to 10 carbon atoms and the

heterocycloalkyl and heterocyclenyl radicals  
comprise 3 to 10 carbon atoms; or  
an optical isomer thereof or a  
pharmaceutically acceptable salt thereof.

- 5
2. The combination according to claim 1, wherein the  
compound of formula (I) is chosen from the  
following compounds:  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
10 (pyrid-3-yl)methylsulfonamide or  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methylsulfonamide, or a  
pharmaceutically acceptable salt thereof.
- 15 3. The combination according to claim 1, wherein the  
product which activates dopaminergic  
neurotransmission in the brain is chosen from the  
following compounds:  
bromocriptine, cabergoline, adrogolide, BAM-1110,  
20 duodopa, levodopa, dopadose, CHF1512, PNU-95666,  
ropinirole, pramipexole, rotigotine, spheramine,  
TV1203, uridine, rasagiline, selegiline, SL340026,  
tolcapone or entacapone.
- 25 4. The combination according to claim 1, wherein the  
product which activates dopaminergic  
neurotransmission in the brain is levodopa and the  
CB1 antagonist is N-{1-[bis(4-  
chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-  
30 yl)methylsulfonamide.
5. The combination according to claim 1, wherein the  
product which activates dopaminergic  
neurotransmission in the brain is ropinirole and  
35 the CB1 antagonist is N-{1-[bis(4-

chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-yl)methylsulfonamide.

- 5 6. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is bromocriptine and the CB1 antagonist is N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-yl)methylsulfonamide.
- 10 7. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is pramixepole and the CB1 antagonist is N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-yl)methylsulfonamide.
- 15 8. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is rasagiline and the CB1 antagonist is N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-yl)methylsulfonamide.
- 20 9. The combination according to claim 1, wherein the product which activates dopaminergic neurotransmission in the brain is entacapone and the CB1 antagonist is N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-yl)methylsulfonamide.
- 25 30 10. The combination according to claim 1, characterized in that the product which activates dopaminergic neurotransmission in the brain is levodopa and the CB1 antagonist is
- 35

N-{1-[bis(4-chloro-phenyl)methyl]azetidin-3-yl}-N-(3,5-difluorophenyl)-methanolsulfonamide.

11. The combination according to claim 1, wherein the  
5 product which activates dopaminergic  
neurotransmission in the brain is ropinirole and  
the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methanolsulfonamide.
- 10 12. The combination according to claim 1, wherein the  
product which activates dopaminergic  
neurotransmission in the brain is bromocriptine  
and the CB1 antagonist is  
15 N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methanolsulfonamide.
13. The combination according to claim 1, wherein the  
20 product which activates dopaminergic  
neurotransmission in the brain is pramipexole and  
the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methanolsulfonamide.
- 25 14. The combination according to claim 1, wherein the  
product which activates dopaminergic  
neurotransmission in the brain is rasagiline and  
the CB1 antagonist is  
30 N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methanolsulfonamide.
15. The combination according to claim 1, wherein the  
35 product which activates dopaminergic  
neurotransmission in the brain is entacapone and  
the CB1 antagonist is

N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(3,5-difluorophenyl)methylsulfonamide.

16. A method of treating Parkinson's disease in a  
5 patient comprising administering to said patient a  
therapeutically effective amount of a combination  
of a product which activates dopaminergic  
neurotransmission in the brain and one or more CB1  
antagonists of formula (I) as defined in claim 1,  
10 optionally in combination with a pharmaceutically  
acceptable carrier.
17. The method according to claim 16, wherein the  
compound of formula (I) as defined in claim 1 is  
15 chosen from the following compounds:  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(pyrid-3-yl)methylsulfonamide, or  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methylsulfonamide, or a  
20 pharmaceutically acceptable salt thereof.
18. The method according to claim 16, wherein the  
product which activates dopaminergic  
neurotransmission in the brain is chosen from the  
25 following compounds:  
bromocriptine, cabergoline, talipexole,  
adrogolide, BAM-1110, duodopa, levodopa, dopadose,  
CHF1301, CHF1512, PNU-95666, ropinirole,  
pramipexole, rotigotine, spheramine, TV1203,  
30 uridine, rasagiline, selegiline, SL340026,  
tolcapone or entacapone.
19. The method according to claim 16, wherein said  
product and said compound of formula (I) as  
35 defined in claim 1 are administered either

simultaneously, separately or spread out over time.

20. A pharmaceutical composition comprising one or  
5 more products which activate dopaminergic neurotransmission in the brain and one or more CB1 antagonists of formula (I) as defined in claim 1 in combination with a compatible and pharmaceutically acceptable vehicle.
- 10 21. The pharmaceutical composition according to claim 20, wherein the compound of formula (I) as defined in claim 1 is chosen from the following compounds:  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
15 (pyrid-3-yl)methylsulfonamide, or  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(3,5-difluorophenyl)methylsulfonamide, or a pharmaceutically acceptable salt thereof.
- 20 22. The pharmaceutical composition according to claim 20, wherein the product which activates dopaminergic neurotransmission in the brain is chosen from the following compounds:  
bromocriptine, cabergoline, talipexole,  
25 adroglide, BAM-1110, duodopa, levodopa, dopadose, CHF1301, CHF1512, PNU-95666, ropinirole, pramipexole, rotigotine, spheramine, TV1203, uridine, rasagiline, selegiline, SL340026, tolcapone or entacapone.
- 30 23. The pharmaceutical composition according to claim 20, wherein the product which activates dopaminergic neurotransmission in the brain is levodopa and the CB1 antagonist is



N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-yl)methylsulfonamide.

24. The pharmaceutical composition according to claim  
5 20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
ropinirole and the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
10 (pyrid-3-yl)methylsulfonamide.
25. The pharmaceutical composition according to claim  
20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
bromocriptine and the CB1 antagonist is  
15 N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(pyrid-3-yl)methylsulfonamide.
26. The pharmaceutical composition according to claim  
20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
pramixepole and the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(pyrid-3-yl)methylsulfonamide.
27. The pharmaceutical composition according to claim  
25 20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
rasagiline and the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
30 (pyrid-3-yl)methylsulfonamide.
28. The pharmaceutical composition according to claim  
35 20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
entacapone and the CB1 antagonist is

N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(pyrid-3-yl)methylsulfonamide.

29. The pharmaceutical composition according to claim  
5 20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
levodopa and the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methylsulfonamide.
- 10 30. The pharmaceutical composition according to claim  
20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
ropinirole and the CB1 antagonist is  
15 N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methylsulfonamide.
31. The pharmaceutical composition according to claim  
20, wherein the product which activates  
20 dopaminergic neurotransmission in the brain is  
bromocriptine and the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
(3,5-difluorophenyl)methylsulfonamide.
- 25 32. The pharmaceutical composition according to claim  
20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
pramixepole and the CB1 antagonist is  
N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-  
30 (3,5-difluorophenyl)methylsulfonamide.
33. The pharmaceutical composition according to claim  
20, wherein the product which activates  
dopaminergic neurotransmission in the brain is  
35 rasagiline and the CB1 antagonist is

N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(3,5-difluorophenyl)methylsulfonamide.

- 5 34. The pharmaceutical composition according to claim 20, wherein the product which activates dopaminergic neurotransmission in the brain is entacapone and the CB1 antagonist is N-{1-[bis(4-chlorophenyl)methyl]azetidin-3-yl}-N-(3,5-difluorophenyl)methylsulfonamide.
- 10 35. The pharmaceutical composition according to claim 20 for a simultaneous use, separate use or use spread out over time.
- 15 36. The pharmaceutical composition according to claim 20 wherein the CB1 antagonist of formula (I) as defined in claim 1 is present in an amount of from about 0.1 mg to about 500 mg.